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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,555	ROMOND ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 10/2/2006 is acknowledged. Claims 4 and 6-16 have been canceled. Claims 1 and 5 have been amended. Claims 1 and 5 have been amended. Claims 1-3 and 5 are pending. The restriction requirement mailed on 6/30/2006 is withdrawn in lieu of Applicant's amendment.

Priority

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in France on July 21, 2000 and October 2, 2000. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter. Accordingly, the application is afforded the instant filing date of November 28, 2003.

Information Disclosure Statement

The information disclosure statement filed 11/28/2003 is acknowledged. However, no copies of the foreign patent documents and non-patent literature publications could be found in the instant application. Accordingly, the form-1449 was not considered by the Examiner. The information disclosure statement will remain in the file until copies of the references cited therein are provided. The Examiner regrets any inadvertent inconvenience.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

3. The disclosure is objected to because of the following informalities:

(a) The disclosure is objected at pages 8-16, 20, 23- 27 because the designation for the sequence identifier is improper (see MPEP§ 2422.03). It is suggested amending the disclosure to recite -- SEQ ID NO: --, not "SEQ ID No.".

Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is "undue". These factors include but are not limited to: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented in the specification, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the unpredictability of the art and (8) the breadth of the claims. (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)) *(MPEP 2164.01(a))*.

The claims of the instant invention are broadly drawn to a method for detecting the elements constituting a bacterial flora, at lease some of the elements of which have an rpoBC operon in common, characterized in that: (a) the genomic DNA of said flora or the mRNAs is (are) prepared, (b) at least some of the noncoding intergenic sequences located in the operon conserved in at least some of the elements of the flora are amplified and the various intergenic sequences amplified are identified in order to determine the elements of said flora. The claims further comprise identifying the amplified sequence by using a DNA kit and providing primers to amplify the intergenic sequences.

At pages 5 and 6, the specification teaches that the present invention is directed to a method for detecting and identifying the elements constituting a microorganism flora, in particular the intestinal flora, according to which a target which is even more discriminatory and universal than those already studied is detected and the sequences of this target characterized and studied using

PCR-like techniques. At page 8, the specification teaches that an operon, which is particularly suitable for implementing the method according to the invention, is the bacterial rpoBC operon. The specification further teaches that is possible to determine degenerate primers for amplifying a region, which is heterologous between species and corresponds to the transcribed intergenic regions. At page 11, the specification teaches that the subject of the invention is also the genomic sequences of microorganisms, which may be amplified by the primers according to the invention. Another operon, which is particularly suitable for implementing the method according to the invention, is the bacterial GroESL operon. At page 13, the specification teaches that it is therefore possible to determine degenerate primers to amplify a region which is heterologous between species and which corresponds to the transcribed intergenic region (IGR).

The specification is not limited to any one bacterial flora or element constituting a bacterial flora and thus it is unpredictable as to whether one of skill in the art could make and use the invention in a manner reasonably commensurate with the instant claims. The specification fails to account for the plethora of bacterial flora encompassed by the claims as broadly written. The specification does not provide any teaching or evidence which suggest that the method is capable of detect any type of bacterial flora such as those directed to an intestinal or colonic bacterial flora; or oral bacterial flora; or bacterial flora of the respiratory tract; or bacterial flora of the skin; or ocular bacterial flora; or urinary bacterial flora; or bacterial flora from different organism and/or species; such as e.g., human versus mammal or fish, or environmental bacterial flora; such as those associated with soil or water; or normal versus pathogenic bacterial flora. Further, neither the claims nor the specification provides a limiting definition as to what constitutes "the elements of a bacterial flora" or provide any evidence or teaching which supports the use of the method for detecting the numerous constituents or elements constituting a bacterial flora as encompasses by the claims as currently

written. For example, the specification teaches at page 1, that it is estimated that the colonic flora of an individual consists of 10^{13} to 10^{15} bacteria, mostly anaerobic bacteria, represented by at least 400 species belonging to approximately 30 different genera. However, there is no teaching anywhere in the specification wherein the 10^{13} to 10^{15} bacteria that makes up a colonic bacterial flora is detected or could be detected using the instant invention. While it is noted that the specification teaches at pages 15-16 that it possible to detect microorganisms of the following genera: Lactococcus, Bifidabacterium, Mycobacterium, Helicobacter, Camplylobacter, Bacteroides, Chlamydia, Mycoplasm, Strephylococcus, Lactococcus and/or Streptococcus, Lactobacillus and/or Bacilus, Clostridium. Enterobacteriaceae, Pasteurella and/or Haemophilus, Neisseria and/or Legionella, Aeromonas and/or Bordetella, Lactobacillus and/or Bacillus, using sequences define therein, the specification does not correlate these microorganism to any one type of bacterial flora and does not provide any teachings which suggest that theses microorganism constitute an element of a bacterial flora as instantly claim. Furthermore, it is again noted that the claims are not limited to any one element or microorganism or bacterial flora and thus further encompasses gene sequences not adequately described or disclosed. The specification and Examples therein beginning at page 22 only teaches two gene sequences rpoBC operon and GroESL operon and isolation of intergenic sequences from said genes as possibly being an element associated with intestinal bacterial flora. The specification however, does not account for the numerous other regulatory and non-regulatory elements or genes, such as e.g., antibiotic resistance genes, transcriptional regulatory gene, housekeeping genes, and etc, that are encompassed in the instant invention as currently written.

Therefore, absent guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. The prior teaches universal targets for identification of species of an organism and the amplification and

identification of highly conserved regions of a heat shock polypeptide in the organism identified (Goh et al, US 5,989,821). The art further provides a small list of bacteria commonly found in the normal flora of humans (Online Textbook of Bacteriology, pages 1-20, http://www.textbookofbacteriology.net/normalflora.html). Other art, examines different species of the genus liberobacter and intergenic regions of ribosomal protein genes associated therewith (Planet et al., Current Microbiology, vol. 30, pages 137-141, 1995). The art however doe not provide a teaching of a method of detecting the elements constituting a bacterial flora commensurate fully in scope as currently claimed by applicant. The art does not provide a teaching wherein every possible microorganism (those known and unknown) that are found in any one type of bacterial flora is identified. Likewise, the art does not teach wherein every regulatory and non-regulatory region or element and gene sequences associated therewith are identified for any one type of bacterial flora. Therefore, further experimentation is necessary to practice the instant invention fully commensurate in scope. Given the high level of skill in the relevant art, it is clear that further experimentation is necessary in order to further identified and detect the elements constituting a desired type of bacterial flora. However, the outcome of such further experimentation cannot be predicted due to the large and diverse sample size and diversity of numerous elements and gene sequences associated with each microorganism of a desired bacterial flora. It is unpredictable as to whether every element constituting a bacterial flora could even be detected due to the large plethora of unknown and uncultivable microorganisms that may be encompassed by a desired flora. Accordingly, it is unpredictable as to whether any quantity of experimentation would be sufficient to allow one skill in the art to use Applicant's invention as now claimed. In view of the foregoing, undue experimentation is deemed necessary to practice the invention fully in scope.

Claim Rejections - 35 USC § 112 second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-3 and 5 are indefinite because the claims are generally narrative and confusing, failing to conform to current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. For example, the claims are confusing at "characterized in that" because it cannot be determined how the claimed scope is affected. It is suggested that typical U.S. claim language be substituted, such as e.g., "wherein".

(b) Claims 1-3 and 5 are vague and indefinite because the claims appear to recite an outcome or desired property, but not any actual, positive method steps. Additionally, such language as e.g., "demonstration of possible hybridization" is not a method step and cannot be construed as such. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion (see *ex parte Erlich*, 3 UsPQ2d1011, p.1011 (Bd. Pat, Applicant. Int.1986). Appropriate correction is required.

(c) Claims 1-3 and 5 are vague and indefinite at "detecting the elements" because the neither the claims nor specification provides any limiting definition of what is considered to be the targeted "element" and it cannot be determined Applicant's intent. Clarification is required.

(d) Claim 2 is indefinite at "carried out on a DNA kit" because a DNA kit is considered to a product comprising components for a desired use. A DNA kit is not considered a method or an apparatus or reaction vessel. Further, neither specification nor claims define what constitutes "a

DNA kit" in the context of the claim language. Therefore, it cannot be determined what process is required for the claim to operate. Clarification is required.

(d) Claim 1 lacks proper antecedent basis for "the noncoding intergenic sequence" because the prior steps do not recited any "noncoding intergenic sequence(s)". It is suggested amending the claims such that the claim language agrees.

(e) Claim 2 lacks proper antecedent basis for " the known element" because the claim 1 from which it depends does not recite any "known element". Clarification is required.

(f) Claim 2 lacks proper antecedent basis for "the sequence liable to be amplified" because the claim 1 from which it depends does not identify such sequence and it cannot be determined Applicant's intent. Clarification is required

(g) Claim 3 lacks proper antecedent basis for "the primer" because the claims 1 and 2 from which the claim depends do not recite any primers. Thus it cannot be determine what applicant is making reference to. Clarification is required.

(h) Claim 3 is confusing and lacks proper antecedent basis for "flanking genes" because the prior steps do not recited or define any "flanking genes" such that it is unclear what reference is being made to. Clarification is required.

(i) Claim 5 is confusing at "at least partially amplified" because the claim 1 from which it depends does not recite any steps of amplification or partial amplification. The claims recite an outcome with no active method steps. Therefore, it cannot be determine what sequences are considered "partially amplified".

(j) Claim 5 is indefinite at the recitation of "IGR" because abbreviations often have more than one meaning in the art. It is suggested amending the claim to recite the full name of the abbreviation as supported by the specification as originally filed.

(k) Claim 5 is confusing and vague for the limitation recited in parentheses "(or homologous genes)" because it cannot be determine if the limitation in parentheses is intended to be an element encompassed by the claim or a separate entity. Clarification is required.

Claim Rejections - 35 USC § 102(b)

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

*Note*** Given the ambiguity of the claims, the preceding rejections are based on the Examiner best interpretation of the claim language. For the purpose of application of prior art, the term "element" is being interpreted as any regulatory or nonregulatory element or gene sequence associated with a mixture of microorganisms.*

8. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Goh et al (US 5, 989,821, November 23, 1999). Regarding claim 1-3, Goh et al teach a method for detecting an elements of a bacterial flora by amplifying a highly conserved region flanking a variable region of a genomic nucleic acid from a mixture of organisms (see figures 1 and 4) by PCR amplification and hybridization techniques (see examples, col. 9-12). Goh et al teach wherein the intergenic sequences of interest are directed to heat shock protein 60 genes (col. 2, lines 33-67 and col. 12, lines 11-60; see also Figures 1-4). Therefore, Goh et al meets the limitation of claims 1-3 of the instant invention.

9. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Planet et al (Current Microbiology, vol. 30, pages 137-141, 1995). Regarding claim 1-3 and 5, Planet et al teach a method of detecting an element of a bacterial flora by amplifying intergenic regions between rpoBC and homologous gene using PCR amplification and hybridization techniques, (see section

entitled "Abstract", "Material and Methods" and "Results", see also Figure 1 and Table 1). Therefore, Planet et al meet the limitation of the claims 1-3 and 5 of the instant invention.

10. Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Dennis, P. (The Journal of Biological Chemistry, col. 259, no. 5, pages 3202-3209, 1984). Regarding claim 1-3 and 5, Dennis teaches a method of detecting an element of a bacterial flora by amplifying intergenic regions between rpoB and rpoC or homologous gene using PCR amplification and hybridization techniques, (see section entitled "Abstract", "Material and Methods" and "Results", see also Table 1, Figures 1 and 3). Therefore, Dennis meets the limitation of the claims 1-3 and 5 of the instant invention.

Art Made of Record

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bergsland and Haselkorn (Journal of Bacteriology, vol. 173, no. 11, pages 3446-3455, 1991) teach a method for detecting an element constituting a bacterial flora by examining via PCR and hybridization techniques intergenic sequences between rpoB and rpoC (see entire reference).

Conclusion

13. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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